PATENT COOPERATION TREATY

REC'D 25 JUL 2005

| From the | | | | | | | |
|---|--|--|-------------------------------|---|-----------------------|-----------|--|
| INTERNATIONAL SEARCHING AUTHORITY | | | | | | WIPO | |
| To: SVETLANA SHTADLER REINHOLD COHN AND PARTNERS P.O. BOX 4060 | | | | PCT | | | |
| TELAVIV, ISRAEL 61040 | | | | WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY | | | |
| | | | | | (PCT Rule 43bis. | .1) | |
| | | | | Date of mailing (day/month/year) 21 JUL 2005 | | | |
| Applicant's or agent's file reference | | | | FOR FURTHER ACTION See paragraph 2 below | | | |
| 157938-2 CC | | | | | | | |
| Internation | nal application No |). | International filing date (| day/month/year) | Priority date (day/mo | nth/year) | |
| | | | 16 January 2005 (16.01.2 | | | | |
| | | , , | or both national classificati | | | | |
| | | C07F 5/00 a | nd US Cl.: 424/1.89, 9.1, 9 | .3, 1.65; 534/14 | | | |
| Applicant | | | | | | | |
| NST NEU | ROSURVIVAL | TECHNOLO: | GIES LTD. | | | | |
| 1. This c | ppinion contains is | ndications rel | ating to the following items | s: | | | |
| | Box No. I | Basis of the | opinion | | | | |
| | Box No. II | Priority | | | | | |
| | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | | | | | |
| | Box No. IV | Lack of unity of invention | | | | | |
| | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | | | | |
| | Box No. VI | Certain documents cited | | | | | |
| | Box No. VII | Certain defects in the international application | | | | | |
| | Box No. VIII Certain observations on the international application | | | | | | |
| 2. FUR | THER ACTIO | N . | • | | | | |
| If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered. | | | | | | | |
| If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. | | | | | | | |
| For further options, see Form PCT/ISA/220. | | | | | | | |
| 3. For further details, see notes to Form PCT/ISA/220. | | | | | | | |
| Name and | mailing address o | f the ISA/ US | <u> </u> | Authorized officer | 100 1 | - / 3 | |
| Mail Stop PCT, Attn: IS A/US Commissioner for Patents | | | Michael G. Hartle | " INTPE | XI + 10 | | |

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Commissioner for Patents
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Alexandria, Virginia 223 13-1450
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Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IL05/00055

| Box No | . I Basis of this opinion |
|--------------------|--|
| i. With re | egard to the language, this opinion has been established on the basis of the international application in the language in which it ed, unless otherwise indicated under this item. |
| | This opinion has been established on the basis of a translation from the original language into the following language, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)). |
| 2. With re inventi | gard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed on, this opinion has been established on the basis of: |
| a. | type of material |
| | a sequence listing |
| | table(s) related to the sequence listing |
| ь. | format of material |
| | in written format |
| . [| in computer readable form |
| c. 1 | time of filing/furnishing |
| [| contained in international application as filed. |
| [| filed together with the international application in computer readable form. |
| [| furnished subsequently to this Authority for the purposes of search. |
| a | n addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished. |
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| orm PCT/IS | A/237(Box No. I) (January 2004) |

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/IL05/00055

| Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | | | | | | |
|---|--------------------|-----|--|--|--|--|--|
| 1. Statement | | | | | | | |
| Novelty (N) | Claims 1-27 | YES | | | | | |
| | Claims NONE | | | | | | |
| Inventive step (IS) | Claims NONE | YES | | | | | |
| | Claims 1-27 | NO | | | | | |
| Industrial applicability (IA) | Claims <u>1-27</u> | YES | | | | | |
| | Claims NONE | NO | | | | | |
| | | | | | | | |

2. Citations and explanations:

Claims 1-27 lack an inventive step under PCT Article 33(3) as being obvious over NST TECHNOLOGIES LTD. ("NST") WO 02/46147 A2. NST discloses methods of selective targeting a compound to a cell undergoing perturbation of the normal organization of its plasma membrane comprising contacting the cells with a labeled compound or conjugate thereby selectively targeting said cell population, see abstract and page 4. The compounds include those which may have a contain a malonic acid derivative moiety, as R1 can be U-D-U, wherein D is a C1-C6 alkylene and U is C(O)O, see pages 4-5 and 14. The compounds may be conjugated to N2S2 chelators, as claimed, to be labeled for methods of imaging. The labels include Tc-99, Gd, etc. for use in various imaging methods, radioimaging, MRI, etc., see page 18+. The compounds may be used for targeting tumors, etc, see page 18+. While NST does not specifically exemplify the same compounds as claimed as used in the claimed methods, it would have been obvious to prepare and use such compounds because NST teaches a broad formula that can be substituted to yield compounds having the same chemical moieties, use and properties as claimed.

Claims 1-27 meet the criteria set out in PCT Article 33(3), because the prior art does not specifically disclose or exemplify the same compounds, having the same formula, as claimed, as used in the claimed methods.

Claims 1-27 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

Form PCT/ISA/237 (Box No. V) (January 2004)